REMARKS/ARGUMENTS

Claims 1-6 and 8-11 are under examination in the application. The Office Action mailed on August 22, 2007 includes the following objections and rejections:

1. Claims 7 and 78 are been rejected under 35 U.S.C. § 112.
2. Claims 1-6 and 8-11 are rejected under 35 U.S.C. §102 as being as anticipated by Pagratis (Pagratis '611).
3. Claims 1-6 and 8-11 are rejected under 35 U.S.C. §102 as being as anticipated by Pagratis (Pagratis '616).
4. Claims 1 and 7 are rejected under 35 U.S.C. §102 as being as anticipated by Rubenfield (Rubenfield).

A response to each of these objections and grounds for rejection follows.

Claim 7 is rejected under 35 U.S.C. § 112 second paragraph.

The Action rejects claim 7 under 35 U.S.C. § 112 as being indefinite and failing to point out and distinctly claim the subject matter that the Applicant regards as the invention.

Applicants submit the claims as filed FULLY comply with the 35 U.S.C. § 112, second paragraph, which demands only the language to be as precise as the subject matter permits and that claims, read in light of the specification, reasonably apprise those skilled in the art of the utilization and scope of the invention. *Shatterproof Glass Corp. v. Libbey Owens Ford Co.*, 758 F.2d 613, 225 USPQ 634 (Fed. Cir. 1985); MPEP 7173.05(a).

The claim uses precise language to define both the structure and the function and when read in light of the specification, a reasonably skilled artisan can use the full scope of the invention. Claim 7 of the instant application states that the aptamer of claim 1 (i.e., that binds to a TGF-beta protein), wherein the aptamer comprises one or more thio-modifications as set forth in the sequence and modifications of SEQ ID NO. 62. Claim 78 of the instant application teaches a partially thio-modified aptamer that binds specifically to TGF-β comprising a sequence

and modifications that is at least 80% complementary to SEQ ID NO: 62. As such, claim 7 and claim 78, FULLY complies with the 35 U.S.C. § 112, second paragraph.

In addition, the Action states:

> Thus, SEQ ID NO: 62 does not have any modifications. For example, would modifications of SEQ ID NO: 62 include sequences with 10%, 20%, 40%, 80%, etc. complementary/identity; would the addition of a thiol to SEQ ID NO: 62 be a modification; would the removal of the thio-modification required by independent claim 1 be considered the modification in claim 7,

Applicant submits that this does not render the claim indefinite and fully complies with 35 U.S.C. § 112 second paragraph. It is not necessary for the application to state specifically what the exact amount to be modified or each and every specific modification, as that is within the scope of the knowledge of the skilled artisan, e.g., see *In re Johnson*, 282 F.2d 370, 373, 127 USPQ 216, 219 (CCPA 1960); *In re Hitchings*, 342 F.2d 80, 87, 144 USPQ 637, 643 (CCPA 1965). See also *In re Brana,* 51 F.2d 1560, 1566, 34 USPQ2d 1437, 1441 (Fed. Cir. 1993). One skilled in the art, based on knowledge of compounds and modifications having similar physiological or biological activity, would be able to discern an appropriate modifications. Therefore, Applicant submits that the claim is not indefinite.

Furthermore, a dependent claim should be construed to incorporate by reference all the limitations of each of the particular claims in relation to which it is being considered and to add a further limitation thereto. As a result, claim 7 and claim 78 cannot remove the limitation (thiol modification of claim 1) would render the claim repugnant to the independent claim and the preamble of the dependent claims.

Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 112.

Claims 1-6 and 8-11 are rejected under 35 U.S.C. §102 as anticipated by Pagratis, et al., U.S. Patent No. 6,346,611 and 6,713,616.

The Action also rejects claims 1-6 and 8-11 under 35 U.S.C. § 102(e) as being anticipated by Pagratis, et al. U.S. Patent No. 6,346,611 and 6,713,616 (hereafter referred to as jointly as "Pagratis" or individually as "Pagratis '611" and "Pagratis '616". Applicants respectfully submit that the cited reference fails to meet the standard of 35 U.S.C. § 102(e) namely, teaching all elements of the claimed invention either explicitly or impliedly and every limitation of the present invention.

Pagratis does not **identically disclose every element** of the claimed invention. See *Corning Glass Works v. Sumitomo Electric*, 9 USPQ 2d 1962, 1965 (Fed. Cir. 1989). A reference that excludes a claimed element, no matter how insubstantial or obvious, is enough to negate anticipation. *Connell v. Sears, Roebuck & Co.*, 220 USPQ 193, 198 (Fed. Cir. 1983). Specifically, Pagratis does not disclose the partial thio-modification of aptamers, that is, to modify some but not all of the links in the backbone at specific locations and their isolation and characterization, as described by the present inventors. Pagratis merely teaches the use of a capping agent.

Furthermore, Pagratis is simply not enabling art. Neither Pagratis nor the reference to SELEX teaches how to make and use backbone modifications or phosphorothioate modifications, that is, to modify some but not all of the links in the backbone at specific locations and their isolation and characterization, as described by the present inventors.

> **One potential problem encountered** in the therapeutic, prophylactic, and in vivo diagnostic use of nucleic acids **is that oligonucleotides in their phosphodiester form may be quickly degraded in body fluids by intracellular and extracellular enzymes** such as endonucleases and exonucleases before the desired effect is manifest. **Certain chemical modifications of the nucleic acid ligand can be made to increase the in vivo stability of the nucleic acid ligand or to enhance or to mediate the delivery of the nucleic acid ligand.** See, e.g., U.S. patent application Ser. No. 08/117,991, filed Sep. 8, 1993, entitled "High Affinity Nucleic Acid Ligands Containing Modified Nucleotides", now abandoned and U.S. patent application Ser. No. 08/434,465, filed May 4, 1995, entitled "Nucleic Acid Ligand Complexes", which are specifically incorporated herein by reference. Modifications of the nucleic acid ligands contemplated in this invention include, but are not limited to, those which provide other chemical groups that incorporate additional charge, polarizability, hydrophobicity, hydrogen bonding, electrostatic interaction, and fluxionality to the nucleic acid ligand bases or to the nucleic acid ligand as a whole. Such modifications include, but are not limited to, 2'-position sugar modifications, 5-

> position pyrimidine modifications, 8-position purine modifications, modifications at exocyclic amines, substitution of 4-thiouridine, substitution of 5-bromo or 5-iodo-uracil, **backbone modifications, phosphorothioate** or alkyl phosphate modifications, methylations, unusual base-pairing combinations such as the isobases isocytidine and isoguanidine and the like. Modifications can also include 3' and 5' modifications such as capping. Pagratis, et al. U.S. Patent No. 6,346,611 column 12 line 58 to column 13 line 20. Pagratis, et al. U.S. Patent No. 6,713,616 column 12 line 60 to column 13 line 23. Emphasis added.

As stated by the Courts in *Akzo N.V. v. ITC*, 1 U.S.P.Q.2d 1241, 1245 (Fed. Cir. 1986) and *Titanium Metals Corp. v. Banner*, 227 U.S.P.Q. 773, 778 (Fed. Cir. 1985), the anticipating prior art reference "must enable one skilled in the art to practice the claimed invention, thus placing the allegedly disclosed matter in the possession of the public." The mere broad listing of different compounds by Pagratis **does not place the partial thio-modification of aptamers** in possession of the public. See additionally, *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 586 F. Supp. 1176, 1221, 222 USPQ 863 (D. Kan. 1984). af'd in part & rev'd in pan, 772 F.2d 1570, 227 USPQ 177 (Fed. Cir. 1985) ("**a printed publication which merely names a new compound or substance is insufficient as an anticipation**.") (emphasis added); *Air Products & Chem.. Inc. v. Chas. S. Tanner Co.*, 219 USPQ 223 (D. S.C. 1983) ("a prior art reference which contains a **broad general disclosure requiring guessing, testing, speculation or 'picking and choosing' from an encyclopedic disclosure will not anticipate**.") (emphasis added). Pagratis simply does not teach how to make and use backbone modifications or phosphorothioate modifications and cannot anticipate the present invention.

Applicants are fully aware that every claim of a patent is presumed valid under 35 U.S.C. § 282. However that presumption does not extend to every broad concept or component merely listing in the patent. As stated by the Courts in *Akzo N.V. v. ITC*, 1 U.S.P.Q.2d 1241, 1245 (Fed. Cir. 1986) and *Titanium Metals Corp. v. Banner*, 227 U.S.P.Q. 773, 778 (Fed. Cir. 1985), the anticipating prior art reference "must enable one skilled in the art to practice the claimed invention, thus placing the allegedly disclosed matter in the possession of the public." See additionally, *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 586 F. Supp. 1176, 1221, 222 USPQ 863 (D. Kan. 1984). af'd in part & rev'd in pan, 772 F.2d 1570, 227 USPQ 177 (Fed. Cir. 1985) ("**a printed publication which merely names a new compound or substance is insufficient as an anticipation**.") (emphasis added); *Air Products & Chem.. Inc. v. Chas. S. Tanner Co.*, 219 USPQ 223 (D. S.C. 1983) ("a prior art reference which contains a **broad general disclosure**

requiring guessing, testing, speculation or 'picking and choosing' from an encyclopedic disclosure will not anticipate.") (emphasis added). The question here is not if the claims of the patent are valid but if the mere mentioning of a broad listing of different compounds by Pagratis places the **partial thio-modification of aptamers** in the possession of the public and enable one skilled in the art to practice the **partial thio-modification of aptamers** of the present invention. Pagratis simply does not teach how to make and use backbone modifications or phosphorothioate modifications and cannot anticipate the present invention.

Neither the '611 patent nor the '616 patent of Pagratis **identically discloses** the claimed invention and Applicants respectfully submit that claims 1-6 and 8-11 are not anticipated. Furthermore, neither the '611 patent nor the '616 patents of Pagratis are enabling and they do not disclose and enable each and every limitation to the present invention. As such, neither the '611 patent nor the '616 patent of Pagratis can anticipation the present invention. The present invention distinctly claims a structure that is different from that in the '611 and '616 patents of Pagratis, namely, that the present invention is directed to partially thio-modified aptamers. Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 102(e).

Claims 1 and 7 are rejected under 35 U.S.C. §102(e) as anticipated by Rubenfield.

The Action also rejects claims 1 and 7 under 35 U.S.C. § 102(e) as being anticipated by Rubenfield, et al., U.S. Patent No. 6,551,795. Applicants respectfully submit that the cited reference fails to meet the standard of 35 U.S.C. § 102(e) namely, teaching all elements of the claimed invention either explicitly or impliedly and every limitation of the present invention.

In order for a rejection under 35 U.S.C. § 102 to be proper, the cited reference must **identically disclose every element** of the claimed invention. See *Corning Glass Works v. Sumitomo Electric*, 9 USPQ 2d 1962, 1965 (Fed. Cir. 1989). A reference that excludes a claimed element, no matter how insubstantial or obvious, is enough to negate anticipation. *Connell v. Sears, Roebuck & Co.*, 220 USPQ 193, 198 (Fed. Cir. 1983).

Applicants respectfully submit that claims 1 and 7 are not anticipated by Rubenfield because it does not **IDENTICALLY** disclose each and every limitation to the present invention and are not enabling; and as such, cannot anticipation the present invention. Rubenfield simply does not teach an aptamer that includes one or more thio-modifications as set forth in the sequence and modifications of SEQ ID NO: 62. The Action states

> For present claims 1 and 7, Rubenfield et al. teach thio-modified nucleic acids with less than 40% identity to present SEQ ID NO: 62 (please refer to the entire specification and SCORE results). Please refer to MPEP § 2112.01which states "Where the claimed and prior art products are identical or substantially identical in structure or composition anticipation or a *prima facie* case of obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433

The citation of the Action makes it clear that the products must be IDENTICAL or SUBSTANTIALLY IDENTICAL in structure. It is unclear how the sequence of Rubenfield **that is less than 40% identity** (as stated by the Action) to the present invention can in any way identically disclose the present invention. A reference that excludes a claimed element, no matter how insubstantial or obvious, is enough to negate anticipation. *Connell v. Sears, Roebuck & Co.*, 220 USPQ 193, 198 (Fed. Cir. 1983). Rubenfield CLEARLY does not **IDENTICALLY** disclose each and every limitation to the present invention and therefore cannot anticipate it.

Applicants fail to understand how a nucleic acid that is only 40% related anticipates the present invention. Furthermore, the oligonucleotide of Rubenfield fails to teach both the structure and function of the present invention, namely, partially thio-modified aptamers that are TGF-beat specific. Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 102(e).

Although the Action states Rubenfield discloses thio-modified proteins. Applicants are unclear of the relevance of the discloser of modified proteins, as the modification of proteins are not relevant to the **partial thio-modification of aptamers** of the present invention. Clarification is requested.

As stated above, Applicants are fully aware that every claim of a patent is presumed valid under 35 U.S.C. § 282. However that presumption does not extend to every broad concept or component merely listing in the patent. As stated by the Courts in *Akzo N.V. v. ITC*, 1 U.S.P.Q.2d 1241, 1245 (Fed. Cir. 1986) and *Titanium Metals Corp. v. Banner*, 227 U.S.P.Q. 773, 778 (Fed. Cir. 1985), the anticipating prior art reference "must enable one skilled in the art to practice the claimed invention, thus placing the allegedly disclosed matter in the possession of the public." See additionally, *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 586 F. Supp. 1176, 1221, 222 USPQ 863 (D. Kan. 1984). af'd in part & rev'd in pan, 772 F.2d 1570, 227 USPQ 177 (Fed. Cir. 1985) ("**a printed publication which merely names a new compound or substance is insufficient as an anticipation**.") (emphasis added); *Air Products & Chem.. Inc. v. Chas. S. Tanner Co.*, 219 USPQ 223 (D. S.C. 1983) ("a prior art reference which contains a **broad general disclosure requiring guessing, testing, speculation or 'picking and choosing' from an encyclopedic disclosure will not anticipate**.") (emphasis added). The question here is not if the claims of the patent are valid but if the mere mentioning of a broad listing of different compounds by Rubenfield places the **partial thio-modification of aptamers** in the possession of the public and enable one skilled in the art to practice the **partial thio-modification of aptamers** of the present invention. Rubenfield simply does not teach how to make and use backbone modifications or phosphorothioate modifications and cannot anticipate the present invention.

Applicants request that the Examiner present evidence for the record how the sequence of Rubenfield that is less than 40% identity to the present invention can identically disclose the present invention or withdraw the rejection.

CONCLUSION

In light of the remarks and arguments presented above, Applicants respectfully submit that the claims in the Application are in condition for allowance. Favorable consideration and allowance of the pending claims is therefore respectfully requested.

If the Examiner has any questions or comments, or if further clarification is required, it is requested that the Examiner contact the undersigned at the telephone number listed below.

Dated: February 22, 2008

Respectfully submitted,

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